[redacted]

From: [redacted]
Sent:
To:

Cc:

Subject: [EXTERNAL] ASCP March Steering Committee Call Minutes
Attachments: [redacted] Steering Committee Call March Minutes.pdf

Dear [redacted] Steering Committee,

Please see the attached [redacted] Steering Committee March Call Minutes. The committee approved four small meeting requests from Alkermes (2), Catalyst Psychiatry Network, and Tonix. Please let me know if you have any concerns by Wednesday, March 14, 2018.

As a reminder, the next scheduled [redacted] Steering Committee Call is **Wednesday, April 04, 2018 from 3:00 PM – 4:00 PM eastern time**.

[redacted]

[redacted]

From: [redacted]
Sent: Thursday, May 30, 2019 2:17 PM
To: [redacted]
Cc:
Subject: ched is the MAPS publication on MDMA we discussed...

Dear [redacted]

> "After screening and enrollment, participants were randomized through a web-based system (MP-8, MP-12) or a list generated by a blinded randomization monitor (MP-1, MP-2, MP-4, MP-9) to receive blinded doses of placebo/control (0 mg placebo; 25 mg, 30 mg, or 40 mg MDMA) or active doses of MDMA(75 mg, 100 mg, or 125 mgMDMA) at approximately 1:2 ratio. Doses were administered during two 8-h psychotherapy sessions spaced 3–5 weeks apart. The initial dose was followed approximately 1.5–2.5 h later by an optional supplemental dose equal to half the initial dose. Participants could accept or decline the supplemental dose, and could discuss the choice with the therapy team. The team could withhold the supplemental dose if there were contraindicating circumstances."

So it looks like the two doses of MDMA were over 6-10 weeks (2x 3-5 weeks)? No 12 week data.

Note that "25 mg, 30 mg, or 40 mg MDMA" was given as an active placebo?

This paper describes studies that are very messy.

[redacted]

From: [redacted]
Sent: Thursday, May 30, 2019 3:02 PM
To: [redacted]
Cc: [redacted]
Subject: Attached is the MAPS publication on MDMA we discussed...

Dear [redacted]

Great to see you and catch up.

As we discussed, attached is the MAPS paper on MDMA. I've got to figure out how long the controlled double-blind phase was.

We are interested in your thoughts.

[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Monday, August 14, 2017 5:54 AM
To: [redacted]
Cc:
Subject: [EXTERNAL] RE: Aurora - Google - Mindstrong

Dear [redacted]

By the way:

https://www.nimh.nih.gov/news/science-news/2016/nimh-funded-study-to-track-the-effects-of-trauma.shtml

[redacted] will lead the study in collaboration with [redacted] These investigators bring the varied expertise necessary for this multi-dimensional study, which will involve screening and recruitment of patients; collecting and storing the wide variety of data and biological samples being collected; analyzing the large volume of data, including genetic findings; and using that data to provide a deeper understanding of the origins of post-traumatic illness. The study has been designed to ensure that data and biological samples can be shared with the field, making possible further analyses by other investigators. Biological samples, for [redacted] NIMH [redacted].

[redacted]

From: [redacted]
Sent: Monday, August 14, 2017 6:53 AM
[redacted]
Subject: Aurora - Google - Mindstrong

Dear [redacted]

We should discuss the project below. I think a study using this device on military-PTSD patients would be well received. Also, we could have the pharmacologic intervention which would provide very meaningful biological data.

This makes sense for the large VA study that you are proposing.

[redacted]

[redacted]

[redacted]

The symptoms of post-traumatic stress disorder include uncontrolled memories of a traumatic event, anxiety and panic—"hyperarousal" is the technical term—depression, avoiding anything that's a reminder of the event, self-destructive behavior, and more. It's the only psychiatric disorder where people are pretty sure of the cause: emotionally traumatic events, from the death of a loved one to an experience of fear or violence. By some estimates 5 to 10 percent of all US adults have PTSD, more women than men. Wars in Afghanistan, Iraq, and other places US troops are deployed put those numbers even higher among people in the military and veterans.

But the biology of PTSD—neurological changes, elevated or depressed levels of something a blood test could pick up, genetic vulnerabilities—is … multifactorial. Difficult to correlate. Under investigation.

Which is to say, nobody's really sure. So this week, a long-in-the-works research study called Aurora is starting to recruit human subjects. Working with 19 hospitals around the country, Aurora will ask 5,000 people to become part of the study. The goal is to try to figure out what biomarkers connect a traumatic event to the development and eventual diagnosis of PTSD.

The researchers at the University of North Carolina and Harvard who are running the study have turned to Verily, the health-focused Google spinoff, for help with data collection and management. That means Aurora will test more than how and why people get PTSD. It'll also test how the methods used to ask scientific questions invariably constrain the answers.

Aurora's design is, without doubt, slick. When eligible people come to an emergency room at one of Aurora's 19 partner institutions, caregivers will try to sign them up. People who agree will, within hours or days of the inciting event, get a baseline biologic and psychiatric assessment, and they'll return for more tests every month. They'll also get a Verily Study Watch, a wearable that captures data like heart rate, skin electrical conductivity, and movement.

If all goes as planned, participants will also get an experimental app on their smartphones from the health startup Mindstrong. By monitoring things like keystroke speed and pressure, speed of word choice while texting, and even simple time on-screen—invisibly, in the background—the Mindstrong algorithms are supposed to be able to pick up early signs and symptoms of psychiatric disorders. It's the "digital phenotype" of an illness.

Right now, no one knows which people who experience trauma are going to develop PTSD, much less how to prevent it or what the underlying biology is. "So we'll get people right after the traumatic event, and then see if six months later they develop one of these outcomes, and then we'll see what's changed," says Sam McLean, director of the Institute for Trauma Recovery at UNC-Chapel Hill and Aurora's principal investigator. "Developing better treatments depends on getting a much deeper, more accurate understanding of what's going on."

A "biomarker" used to be something that only a blood test or imaging like an MRI would find—a physical manifestation of an illness or injury. Aurora expands that definition. "Historically in studies you'd just get snippets of data. Come in for an assessment, fill out forms, take some physiological data. This is getting data in real time," McLean says. That means they can look for patterns. Does a person panic every time they leave the house? In that case, "the biomarker is some combination of GPS and, from the watch, seeing your heart rate spike."

With 5,000 people spewing 24/7 data, you can see why partnering with Verily makes sense. Aurora got $21 million from the National Institutes of Health to spin up; that's not a lot for a big, multicenter, prospective study. So they can take advantage of Verily's Google-spawned data-handling heritage, "keeping track of the data and ensuring it's intact, secure, and well-organized," says Menachem Fromer, Verily's mental health science lead, and using Verily's skill with analytics

and machine learning. Aurora also gets to take advantage of Mindstrong's clever data collection and interpretation algorithms.

Meanwhile Verily and Mindstrong both get to play with the Aurora database to validate and improve their own work. (Verily also has a separate effort, Project Baseline, that will use its watch to monitor 10,000 otherwise healthy people.) "Validation, while it seems straightforward, is actually a really hairy problem," says Tom Insel, a neuroscientist, ex-director of the National Institute of Mental Health, and currently a partner at Mindstrong. "We've got a novel, objective measure of mood and cognition. So how do we prove that?"

In fact, that's exactly what Insel tried to codify when he was head of NIMH, where he championed finding those more objective measures. As Insel himself acknowledged, it didn't quite work—and the attempt polarized the mental health community. Insel left NIMH in 2015 for what was then called Google Life Sciences ... now known as Verily. Then in May he left Verily for Mindstrong.

Both companies hope to help people, and also sell products—not that there's anything wrong with that. But explicitly looking for PTSD biomarkers that might provide therapeutic hooks could also pose a forest/trees problem, because mental health in general doesn't have clearly-defined objective measures of its disorders. "That has made the hunt for biomarkers particularly difficult," says epidemiologist Sandro Galea, dean of the Boston University School of Public Health and chair of a committee that produced an Institute of Medicine report on PTSD in 2014, "You can have PTSD in many different ways," Galea says, "because the diagnostic criteria are essentially a mix of different symptoms and categories."

Big data approaches like what Verily and Mindstrong bring to Aurora have a chance to unify the belts, as it were, collecting huge amounts of information and then sorting through it to try to quantify the qualitative standards. It could be a powerful approach, says Galea, and may well add to knowledge about and the potential to treat PTSD, "but it also introduces a distorting force. Not the data itself—data is value-neutral. But the data applications have what the companies hope are clear commercial approaches."

In other words, if you go looking for biomarkers, you are actually looking for therapeutic targets, and while those targets might be hittable by a drug, they might also oversimplify the actual disorder. It's a step away from holistic theories that try to encompass socioeconomic or public health-style approaches—because, fundamentally, it's easier to sell a drug.

Verily's people understand this potential pitfall, of course. "The best information, to a person living in a social environment that is not that healthy, may not be that useful," former FDA commissioner Robert Califf, now at Verily, said at a recent biotech conference—not talking about PTSD specifically, but health in general. "Social determinants far outweigh the biological determinants."

Aurora's investigators know that working with big-data companies means they have to strike a balance, too. And it's worth it. "They have been and are being terrific," McLean says. "Personally, as PI, if some other entity maybe wouldn't do direct patient assessment but had another way to analyze data or to bring discoveries faster, then hey, I'm totally game." Right now, Aurora, Verily, and Mindstrong have aligned but not equivalent reasons for wanting to bridge the cause-to-symptom gap for PTSD. For people with the disorder, maybe those reasons don't matter, as long as they get results.

[redacted]

From: [redacted]
Sent: Wednesday, February 20, 2019 6:49 AM
To: [redacted]
Cc: [redacted]

[redacted] [EXTERNAL] RE: Slides to AV this morning
Attachments: [redacted]

Hi [redacted]

Here are my final slides for this afternoon. Thanks.

Kind regards,

[redacted]

From: [redacted]
Sent: Wednesday, February 20, 2019 7:30 AM
To: [redacted]
Cc: [redacted]
Subject: Re: Slides to AV this morning

Dear All,
Thanks for this, but I see that the duration of my talk is 20 min + 25 min discussion.

Originally it was 30 min + 15 min discussion. Was it changed? Or is it a mistake?
Actually, I prepared a 30 min presentation, as in the slides I sent you a couple of weeks ago, thus I would ask to speak for at least 25 min.
Thanks.
See you later.
Fabrizio

[redacted]

[redacted] 20 feb 2019 alle ore 11:46 [redacted]

> Hello All,
>
> Because the AV team will be turning the room during the Annual Business luncheon (transition from the parallel to general session set), it would be great if you could get your slides for this afternoons session to them this morning before the start of the parallel sessions. Please take flash drive to tech desk in BALLROOM 2 (Right entrance). [redacted] should be in there.
>
> Thanks a lot!
>
> Best regards,

[redacted]

[redacted]

From: [redacted]
Sent: Wednesday, February 14, 2018 12:10 PM
To: [redacted]
Subject: RE: [EXTERNAL] RE: call today

[redacted]

-----Original Message-----
From: [redacted]
Sent: Wednesday, February 14, 2018 1:05 PM
To: [redacted]
Subject: RE: [EXTERNAL] RE: call today

I will call you at 4pm. What is your cell number

[redacted]

[redacted]
From: [redacted]
Sent: Wednesday, February 14, 2018 10:00:14 AM
To: [redacted]
Subject: [EXTERNAL] RE: call today

Dear [redacted]

I can speak 4-7 pm ET today. I'm on my cell. How long is the review cycle?

[redacted]

From: [redacted]
Sent: Wednesday, February 14, 2018 12:57 PM
To: [redacted]
Subject: call today

[redacted], can I catch up with you about my call with [redacted] that I had this morning.

May be that we submit to Merit grant (March 15 deadline) with the proposal to partner with CSP Coordinating Center, more sites, accelerated timeframe.

Thanks.

[redacted]

From: [redacted]
[redacted] Tuesday, October 31, 2017 12:29 PM
To: [redacted]
[redacted]
Subject: [EXTERNAL] RE: Do you use VINCI?

Dear [redacted]

Great. Yes, let's speak in early December. We are STILL trying to engage Mindstrong/Verily/Calico for the actigraphy. I think we would be well advised to propose collecting biological material for genomic analysis and also some biometrics like actigraphy or home EEG to make it more scientifically intriguing for the reviewers.

Best, [redacted]

[redacted]

From: [redacted]
Sent: Monday, October 30, 2017 10:35 AM
To: [redacted]
Cc: [redacted]
Subject: RE: Do you use VINCI?

Yes, we are able to pull down a patient list and send letter or flyers directly to the veterans living within certain zip codes (all this is done under an IRB-approved HIPAA waiver for purposes of recruitment).

Let's plan a call in early Dec to dust off the multisite study.

Hope your current study is going along well.

Regards,

[redacted]

[redacted]

From: [redacted]
Sent: Monday, October 30, 2017 7:35 AM
To: [redacted]
Subject: [EXTERNAL] Do you use VINCI?

Dear [redacted]

I recently spoke with [redacted] from [redacted]. He told us about a recruitment database available to VA researchers called VINCI. Are you familiar with it? Do you use it? If not, we can connect you with [redacted] and his colleague [redacted] to take you through the system and it's potential for patient recruitment. [redacted] organization covers all the VA non-profits, so it could be useful in a multi-center study like what you're contemplating. He's a very good guy and has connections to other money and resources.

Let's find a time to talk about the new grant proposal.

[redacted]

[redacted]

From: [redacted]
Sent: Friday, March 23, 2018 2:04 PM
To: [redacted]
Cc:
Subject: [EXTERNAL] Encouraging legislation
Attachments: hrpt-115-hr-fy2018-milcon.pdf

Dear [redacted]

With the President's signature this afternoon, please note that the Joint Explanatory Statement accompanying H.R. 1625, the Fiscal Year (FY) 2018 Consolidated Appropriations Act, incorporates by reference the provisions on post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI) previously included in the House Appropriations Committee Report (House Report 115-188 - attached) on FY 2018 appropriations for the Department of Veterans' Affairs (VA).

Encouraging!

[redacted]

[redacted]

From: [redacted]
Sent:
To: [redacted]
Subject: RE: [EXTERNAL] RE: FDA meeting in June

Thank you, [redacted] I look forward to meeting with you next week in Scottsdale.

From: [redacted]
Sent: Monday, May 20, 2019 4:35 PM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] RE: FDA meeting in June

[redacted]

[redacted]

From: [redacted]
[redacted] May 19, 2019 3:50 PM
To: [redacted]
Subject: RE: [EXTERNAL] RE: FDA meeting in June

Dear [redacted]

Please remind me how we should describe you in the attendee list: "[redacted]"?

Would you prefer your university affiliation?

[redacted]

From: [redacted]
Sent: Saturday, May 18, 2019 3:10 PM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] RE: FDA meeting in June

August 1 is much better for me. Yes, and thanks for including me. [redacted]

[redacted]

From: [redacted]
Date: Saturday, May 18, 2019, 4:05 AM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] RE: FDA meeting in June

Dear [redacted]

The date of our FDA meeting was changed to August 1 at noon. Will you be able to come with us?

[redacted]

From: [redacted]
Sent: Wednesday, April 24, 2019 7:01 PM
To: [redacted]
Cc: [redacted]
Subject: RE: FDA meeting in June

I will look at the dates and get back to you. Thanks!

From: [redacted]
Sent: Tuesday, April 23, 2019 1:25 PM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] FDA meeting in June

Dear [redacted]

Our FDA meeting to defend Breakthrough Therapy designation will be held on June 20 at 10 am. Please let me know if you will be able to join us at the meeting.

[redacted]

[redacted]

From: [redacted]
Sent:
To: [redacted]
Subject: [EXTERNAL] Thursday, February 1, 2018 10:30 AM-11:30 AM (UTC-05:00) Eastern Time (US & Canada).

Dear [redacted]

Are you available to join a call with [redacted] and me on Thursday at 10:30 am?

[redacted]

We'll have a follow-up call soon if this time doesn't work for you.

[redacted]

[redacted]

From: [redacted]
Sent: Monday, February 18, 2019 5:55 PM
To: [redacted]
Cc: [redacted]

Subject: [redacted] slides RE: [EXTERNAL] Re: Follow-up Actions for speakers: 22 Jan ISCTM Finding the Signal n Draft Slide Review
Attachments: ISCTM Slide Template Master-Widescreen[redacted].pptx

[redacted]

Attached are my slides for the meeting. So sorry for the delay.

I look forward to the discussion and panel.

Thank you,

[redacted]

From: [redacted]
Sent: Wednesday, January 23, 2019 3:10 PM
To: [redacted]

Subject: [EXTERNAL] Re: Follow-up Actions for speakers: 22 Jan ISCTM Finding the Signal Session Draft Slide Review

Hi [redacted]:

I think this looks great and have no edits.

[redacted]

On Tue, Jan 22, 2019, 4:49 PM [redacted] wrote:

> I am attaching the revised abstract for the panel and welcome edits from the chairs and co-panelists.
>
> Thank you.

[redacted]

[redacted]

From: [redacted]
Sent: Tuesday, January 22, 2019 12:57 PM
[redacted]
Cc: [redacted]
Subject: [EXTERNAL] Follow-up Actions for speakers: 22 Jan ISCTM Finding the Signal Session Draft Slide Review

Dear Speakers,

Thanks to each of you for your time and valuable discussion to develop the session today. Per today:

- Now- Outstanding abstracts due to [redacted]
- 5 Feb: Draft Slides due to Chairs and [redacted] for chair input and so [redacted] and [redacted] can prepare regulatory talks
- Final slides are due on a flash drive no later than 30 minutes before beginning of session- at the AV/registration desk to maintain version control.
- The slide template attached is not required but helps with the non-competitive space we try to maintain. If you use your own slide template, please use widescreen version and have logo only on the first/ disclosure slide. Disclosure slide is required.
- Please visit the Speakers' Corner to fill out your Speaker Confirmation and Agreement if you have not done so already.

Best,

[redacted]

[redacted]

-----Original Appointment-----
From: [redacted]
Sent: Monday, January 14, 2019 6:08 PM
To: [redacted]
Subject: 22 Jan ISCTM Finding the Signal Session Draft Slide Review- 11a EST
When: Tuesday, January 22, 2019 10:00 AM-11:00 AM (UTC-06:00) Central Time (US & Canada).
Where: WebEx and Telecon

Tuesday, January 22, 2019 11:00 am, Eastern Standard Time (New York, GMT-05:00)
Event number: [redacted]
Event password: [redacted]
To join the online event
---
1. Click here to join the online event.
Or copy and paste the following link to a browser:

[redacted]

2. Click "Join Now".

To join the audio conference only

[redacted]

[redacted]

From: [redacted]
Sent:
To: [redacted]
Cc:
Subject: [EXTERNAL] Just spoke to [redacted]

Dear[redacted]

I hope all's well. We just spoke to [redacted] about the CSP, etc. Long story. Let's catch up on the phone. What are good times?

[redacted]

[redacted]

Sent: Saturday, January 20, 2018 4:50 PM
To: [redacted]
Cc:
Subject: [EXTERNAL] Another angle on a new study - high risk suicidal patients

Dear [redacted]

We met with [redacted] on Friday, who's one of the authors of the [redacted] and who's devoted her life to promoting its use.

She thinks that FDA is prepared to look at registration studies for drugs that include patients with [redacted] 4 and 5. She believes from her conversations with [redacted] (head of psych division) that (1) [redacted] can adequately monitor risk, (2) [redacted] can be an endpoint for suicidal ideation and suicidal behaviors and (3) if a patient in trial committed suicide – that it would not be the death knell for that drug because FDA is willing to acknowledge the risk of studying these patients.

Therefore, one of the very big differentiators of a new, big Cooperative study, from our ongoing Phase 3 program, would be to open the study protocol to higher risk patients.

What do you think?

We think that if we also collected biomarkers and a lot of other information, the new study could be a landmark study and possibly shed light on not only PTSD but on suicidal ideation and behaviors.

[redacted]

[redacted]

From: [redacted]
Sent: Monday, April 15, 2019 7:00 AM
To: [redacted]
Subject: [EXTERNAL] FW: High suicide rate among veterans remains unchanged

More reason to study IPS for returning vets.[redacted]

From: [redacted]
Date: Monday, April 15, 2019 at 7:54 AM
To: [redacted]
Subject: High suicide rate among veterans remains unchanged

If you are unable to see the message or images below, click here to view

Good morning. Here are today's top stories.
April 15, 2019

Leading the News

High suicide rate among veterans remains unchanged

The **New York Times** (4/14, Steinhauer) reports, “Three veterans killed themselves last week on Department of Veterans Affairs health care properties, barely a month after President Trump announced an aggressive task force to address the unremitting problem of veteran suicide.” The Times says the “executive order was a tacit acknowledgment of what the deaths rendered obvious: The department has not made a dent in stemming the approximately 20 suicide deaths every day among veterans.” The article adds that “veterans are in many ways an amplification of the same factors that drive suicide in the broader American population: a fragmented health care system, a shortage of mental health resources, especially in rural areas, a lack of funding for suicide research and easy access to guns.”

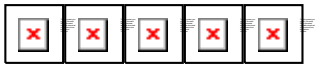
Family picnic or walk-in clinic? What to do when family asks for care
Requests for care from relatives are exceedingly common. The right response preserves the relationship while making sure the person gets good care. **Read more from the AMA**.

HTN guideline sparks clinics' push for accurate BP measurement
This health system had thousands of patients with hypertension when the 2017 ACC/AHA guideline came out. Learn how they adjusted to push their BP-control rate to 83%. **Read more from the AMA**.

ICYMI » 6 mistakes to avoid when starting your private practice
Anticipating pitfalls is a fundamental part of the clinical side of medicine. Any physician opening a private practice should apply that same thinking to establishing their business. Find out what it's like from a doctor who has done it. **Read more from the AMA**.

2019 American Medical Association Annual Section Meetings
Join hundreds of your colleagues from June 6-8 in Chicago to discuss issues affecting health care. It's an opportunity to influence our advocacy agenda on behalf of all patients and physicians, learn from experts during numerous educational sessions on medicine's hottest topics and network with your peers and leaders in the medical community. **Register now**.

Visit the AMA website



HEALTH COVERAGE AND ACCESS

Patients, physicians push for broadened Medicare coverage for CAR-T

The **New York Times** (4/13, Pear) reported that "cancer patients, doctors and drug companies are urging the Trump administration to remove the restrictions and broaden coverage so more patients can benefit from the treatment, known as CAR T cell therapy, or CAR-T," but "insurance companies are pushing for the restrictions." Medicare's final decision "will influence commercial insurers and state Medicaid programs, which often follow its lead." The FDA "has approved two CAR-T products to treat certain blood cancers: Kymriah [tisagenlecleucel]...with a list price of $373,000 or $475,000, depending on the type of cancer, and Yescarta [axicabtagene ciloleucel]...with a list price of $373,000."

QUALITY AND SAFETY

Contaminated endoscopes have caused three deaths, 45 infections, FDA says

CNN (4/12, Goldschmidt) said on its website that "three people died and 45 people developed infections from contaminated endoscopes, the... Food and Drug Administration said Friday." The reports of contamination are specifically associated "with a side-viewing duodenoscope used for a medical procedure called endoscopic retrograde cholangiopancreatography or ERCP." The FDA's report stated, "These reports indicate that although the number of reports has declined, there continues to be a need for improvement of the safety of reprocessed duodenoscopes." Jeff Shuren, M.D., director of the FDA's Center for Devices and Radiological Health, said that the agency is "continuing to evaluate the benefit-risk profile of these devices, and we'd like to see strong evidence that proper cleaning and reprocessing can virtually eliminate any bacteria residue that can spread infections. Currently, that evidence is lacking, and we're considering what additional regulatory actions may be necessary."

Nursing homes, hospitals combat superbugs with special soap

Kaiser Health News (4/12, Gorman) reported that nursing homes and hospitals are "washing patients with a special soap" in an effort to combat superbugs. The efforts, which are being funded "with roughly $8 million from the federal government's Centers for Disease Control," are "taking place at 50 facilities in those two states." Rush University Medical Center infectious-diseases specialist Michael Lin, M.D., said that CREs have "basically spread widely" in Chicago health care facilities, adding, "If MRSA is a superbug, this is the extreme – the super superbug."

PUBLIC HEALTH

Canagliflozin appears to prevent or slow kidney disease, study indicates

The **AP** (4/15, Marchione) reports that the drug Invokana (canagliflozin), a medication "used to help control blood sugar in people with diabetes, has now been shown to help prevent or slow kidney disease." The **findings** were presented at a medical meeting and published online in the New England Journal of Medicine.

Many cancer patients said they do not tell physicians about alternative medicine usage

TIME (4/12, Ducharme) reported that "about a third of cancer patients use alternative medicine – but many of them don't tell their doctors, according to a **new research letter** published in JAMA Oncology." TIME explained that this is "potentially a problem, since alternative therapies can come with health risks, especially if people halt conventional treatments to pursue them." In addition, "some complementary therapies" were said to be "not well-regulated and may interact poorly with conventional treatments like chemotherapy and radiation, doctors warn."

Female firefighters less likely to have health needs addressed, researchers say

Reuters (4/12, Crist) reported on a **study** in Women's Health Issues that found that female firefighters "are less likely to have access to female-specific personal protective equipment and appropriate strength training

and conditioning support," particularly in North America. The researchers "surveyed 840 female firefighters from 14 countries, including the UK, U.S., Canada, Australia and mainland Europe, in 2018," finding that 75 "percent of female firefighters in the U.S. and Canada said they don't have access to female-specific personal protective equipment. Although the numbers are better in the UK, about a third of women don't have a full female kit."

Analysis examines why some people are diagnosed with multiple cancers

In an analysis, the **Washington Post** (4/14, Cimons) reports that "many people assume that when cancer shows up following an earlier tumor, it is a metastasis from the first," but "multiple primary cancers can arise by themselves, and researchers in recent years have begun to unravel some of the reasons." Stephen J. Chanock, director of the division of cancer epidemiology and genetics at the National Cancer Institute, said that as cancer survivors "live longer lives, some of them go on to develop second cancers, tumors unrelated to their original cancer." Some "experts believe that many of these additional primary tumors are the result of earlier treatments for" previous cancers. DNA damage from radiation and chemotherapy "can prompt new cancers to develop later."

Colorectal cancer rates increasing among people under 50

The **Washington Post** (4/12, Berger) reports "colorectal cancer incidences and deaths have been increasing in the past 30 years in people under 50," despite an overall decline. In response the "American Cancer Society recently recommended lowering the screening age to 45," but "health-related professional organizations such as the U.S. Preventive Services Task Force and the Centers for Disease Control and Prevention have yet to adopt them."

Some schools turning away unvaccinated students

The **Wall Street Journal** (4/13, Hobbs, Subscription Publication) reported that with the measles outbreak spreading rapidly in some states, certain school districts are turning away unvaccinated students from campuses where cases of measles have been confirmed. Some states are considering legislation that would make getting vaccination exemptions harder.

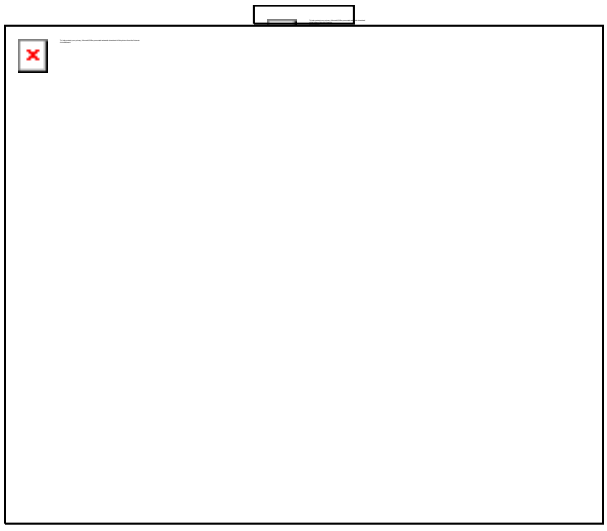
PHARMA & DEVICE UPDATE

FDA approves erdafitinib as first targeted therapy for advanced bladder cancer

Reuters (4/12) reported that "Balversa [erdafitinib] won U.S. approval as the first targeted therapy for advanced bladder cancer, the Food and Drug Administration announced." The medication "is approved for use in patients whose cancer has progressed during or after chemotherapy and have specific genetic alterations known as FGFR3 or FGFR2."

MedPage Today (4/12, Ingram) reported that the agency "warned of the risk of serious eye problems, and said patients should receive eye exams while on treatment."

ALSO IN THE NEWS



AMA launches new project with Sling Health to integrate physician perspectives into new technology development

Modern Healthcare (4/12, Cohen, Subscription Publication) reported, “The American Medical Association has launched a new project with Sling Health, a national biotechnology incubator, in an effort to” quickly “integrate physician perspectives into new technology development.” The project, “called the Clinical Problem Database,” was debuted “on the AMA’s Physician Innovation Network, an online forum that connects physicians with digital health companies seeking clinician feedback.” In a statement, Michael A. Tutty, Ph.D., AMA group vice president of professional satisfaction and practice sustainability said, “Gaining insights from physicians will help make medical technology an asset, not a burden.”

FierceHealthcare (4/12, Landi) reports that Tutty also said, “Physicians and entrepreneurs are passionate about transforming health care, and by engaging collaboratively they can advance innovation that makes the health system work better for everyone. ... Through our collaboration with Sling Health, the AMA is helping physicians and medical students take on a greater role in driving technology forward that responds to real clinical needs.”

FRIDAY'S LEAD STORIES

- **CDC report links Kratom to 91 deaths over 18-month period**
- **AMA says policy banning transgender people from military is unfair and unscientific**
- **FDA launches hand sanitizer ingredient investigation**
- **NASA twins study shows impact of time spent in space**
- **Study finds men who eat greater amounts of meat may be more likely to die prematurely**
- **FDA says women taking flibanserin need not completely avoid alcohol**

Distributed on behalf of:
American Medical Association
330 N. Wabash Ave., Suite 39300
Chicago, IL 60611-5885
(312) 464-5000

[redacted]

From: [redacted]
Sent: Tuesday, February 6, 2018 2:58 PM
To: [redacted]
Cc:
Subject: [redacted]

Just [redacted] and me and [redacted] (copied).

[redacted]

From: [redacted]
Sent: Tuesday, February 6, 2018 3:03 PM
To: [redacted]
Subject: RE: I sent email to [redacted]

Do you have anyone else from your company that needs to be on the VA conf call within the next couple of weeks

[redacted]

From: [redacted]
Sent: Tuesday, February 06, 2018 11:10 AM
To: [redacted]
Subject: [EXTERNAL] RE: I sent email to [redacted]

Okay, great. Keep us posted.

[redacted]

From: [redacted]
Sent: Tuesday, February 6, 2018 11:59 AM
To: [redacted]
Subject: I sent email to [redacted]

Asking for a date for us to meet face-to-face in Feb; his out of office reply says he is out today, but maybe he will respond today or tomorrow.

[redacted]

From: [redacted]
Sent: Wednesday, February 20, 2019 9:16 AM
To: [redacted]
Subject: RE: I will be in DC Tues through THursday this week

Yes

[redacted]

From: [redacted]
Date: Wednesday, Feb 20, 2019, 9:41 AM
To: [redacted]
Cc: [redacted]
Subject: RE: I will be in DC Tues through THursday this week

[redacted]
Can you do 10:30 call with [redacted] If so, I'll set up a VANTS.

From: [redacted]
Sent: Wednesday, February 20, 2019 8:19 AM
To: [redacted]
Cc: [redacted]
Subject: RE: I will be in DC Tues through THursday this week
I am available between 1030 and noon ET

[redacted]

From: [redacted]
Date: Wednesday, Feb 20, 2019, 7:34 AM
To: [redacted]
[redacted] this week
[redacted]
Federal government closed. We are on mandatory telework. I will defer to [redacted] for her availability – I am happy to join a call at a time that works for her.

From: [redacted]
Sent: Tuesday, February 19, 2019 11:49 PM
To: [redacted]
Subject: RE: I will be in DC Tues through THursday this week
Ok, willing to play it by ear or talk by phone.

[redacted]

From: [redacted]
Date: Tuesday, Feb 19, 2019, 7:51 PM
To: [redacted]
Cc: [redacted]
Subject: RE: I will be in DC Tues through THursday this week

[redacted]

You may be aware that we are expecting snow in the AM. I was hoping that it might be minimal but just got an alert that the commuter train from my neck of the woods will be running on a limited schedule tomorrow. So, I'm becoming concerned about my ability to get to DC tomorrow - just a heads up - let's see how things look in the AM.

[redacted]

From: [redacted]
Date: Tuesday, Feb 19, 2019, 5:28 PM
To: [redacted]
Subject: RE: I will be in DC Tues through THursday this week

Yes, I can meet you for coffee Wednesday morning, I need to be at my meeting at noon at [redacted] which is close to [redacted]. You might not get this email until you get into work tomorrow morning, just let me know best time and location and I will come over to meet with you, hopefully both of you!

[redacted]

From: [redacted]
Date: Tuesday, Feb 19, 2019, 6:48 AM
To: [redacted]
Subject: RE: I will be in DC Tues through THursday this week

Hi [redacted]

Thanks for the heads up. I have a pretty good schedule tomorrow/ Wednesday with the exception of 1230 meeting. Tuesday and Thursday this week are really not possible for me. Should we try for morning coffee Wednesday?

[redacted]

[redacted]

From: [redacted]
Date: Monday, Feb 18, 2019, 1:52 PM
To: [redacted]
Subject: I will be in DC Tues through THursday this week

I will be traveling to DC tomorrow afternoon for a meeting at the [redacted] and leaving Thursday. Would either of you be in available to meet for coffee? Other than catching up, I need to chat about proposal with TONIX (but we can do that by phone if you are not able to meet). Would love to see you, [redacted]

From: [redacted]
Sent: Friday, February 15, 2019 3:24 PM

To: [redacted]

Cc: [redacted]

Subject: RE: HOLD: PPI Workshop #2

Thank you all for volunteering in the first place, we are very grateful you would have taken this on!

[redacted]

From: [redacted]

Sent: Friday, February 15, 2019 3:36 PM

To: [redacted]

Cc: [redacted]

Subject: RE: HOLD: PPI Workshop #2

I think this makes sense

-----Original Appointment-----

From: [redacted]

Sent: Friday, February 15, 2019 12:11 PM

To: [redacted]

Subject: Canceled: HOLD: PPI Workshop #2

When: Tuesday, May 14, 2019 12:00 AM to Thursday, May 16, 2019 12:00 AM (UTC-05:00) Eastern Time (US & Canada).

Where: Chicago

Importance: High

Hello all!

After receiving LOIs for this round, we received a significantly smaller # than last time. After speaking with some of the executive committee, it was decided that it didn't make sense at this time to hold this workshop as planned. We will be giving guidance to at least some of the investigators who submitted ideas, but at this time, what that looks like it still being developed.

As we know that the workshop at least wasn't happening, I wanted to let you all know so your calendars could be freed up.

Let me know if you have any questions,

[redacted]

[redacted]

From: [redacted]
Sent: Friday, November 2, 2018 11:15 AM
To: [redacted]
Subject: [redacted]

Attachments: 2018-10-31_Tonix_Pharmaceuticals_Announces_Innovative_Design__1121.pdf

Hi All,
I wanted to share this update with you prior to our call on Monday, although you may have already seen this.

Have a great weekend,
[redacted]

From: [redacted]
Sent: Wednesday, October 31, 2018 8:27 AM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] FW: Tonix Pharmaceuticals Announces Innovative Design in Next Phase 3 Study of Tonmya® for PTSD, Following FDA Meeting

Dear [redacted]

We just announced (see below/attached) the results of a productive FDA meeting, in which FDA agreed to a 4 week primary endpoint in a 12 week study of civilian + military PTSD with trauma ≤ 9 years prior to screening. We plan to start the study in Q1. Four weeks is a better endpoint because there are fewer drop-outs. Both Phase 2 and Phase 3 had p-values < 0.05 at 4 weeks in the mITT populations.

Please suggest times for a call to discuss.

[redacted]

From: [redacted]
Sent: Wednesday, October 31, 2018 7:01 AM
To: [redacted]
Subject: [redacted]

Tonix Pharmaceuticals Holding Corp. has just released the following news:

Tonix Pharmaceuticals Announces Innovative Design in Next Phase 3 Study of Tonmya® for PTSD, Following FDA Meeting

Click here to read the full article

If you have any questions, or would like to contact Investor Relations, please reply to this email.

Tonix Pharmaceuticals Holding Corp.
509 Madison Avenue, Suite 306, New York, NY 10022 United States of America
https://www.tonixpharma.com

[redacted]

[redacted]

Sent: Friday, January 26, 2018 12:01 PM

To: [redacted]

[redacted] Just had lunch with…

…[redacted] I believe the follow-up will be a meeting with [redacted]

[redacted]

[redacted]

From: [redacted]
Sent:
To: [redacted]
Subject:

[redacted]

[redacted]

From: [redacted]
Sent:
To: [redacted]
Cc:
Subject: [EXTERNAL] Attached is the MAPS publication on MDMA we discussed...
Attachments: [redacted]_2019_31065731.pdf

Dear [redacted],

Great to see you and catch up.

As we discussed, attached is the MAPS paper on MDMA. I've got to figure out how long the controlled double-blind phase was.

We are interested in your thoughts.

[redacted]

[redacted]

From: [redacted]
Sent: Tuesday, May 28, 2019 11:24 AM
To: [redacted]
[redacted] Candace Flint
Subject: RE: [EXTERNAL] Meeting at ASCP

Trying to get a reservation at the Ironwood American Kitchen for 7:30AM, but open table wouldn't work on the plane. Will call them once landed then confirm with you.

Best
[redacted]

[redacted]

From: [redacted]
Sent: Tuesday, May 28, 2019 8:33 AM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] Meeting at ASCP

I will aim to meet you at 730 (in running clothes). Where do you want to meet

[redacted]

From: [redacted]
Date: Tuesday, May 28, 2019, 7:59 AM
To: [redacted]
Cc: [redacted]
Subject: Re: [EXTERNAL] Meeting at ASCP

Dear [redacted]

Yes! We want to go the the regulatory plenary.

I can't run with you this year because I'm nursing a sore heel.

[redacted]

[redacted]

On May 28, 2019, at 7:40 AM, [redacted] wrote:

Ok, I was planning to do the fun run at 630, so we can eat breakfast afterwards

Are y'all trying to make it to the 830 regulatory plenary

[redacted]

From: [redacted]
Date: Tuesday, May 28, 2019, 7:07 AM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] Meeting at ASCP

Hi [redacted]

How is tomorrow (Wed) morning for breakfast to meet with me and [redacted] at the meeting?

Best,
[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Wednesday, December 5, 2018 2:36 PM
To: [redacted]
Cc:
Subject: Call me please

Could one of you give me a call about your results? [redacted] Thanks [redacted]

[redacted]

From: [redacted]
Sent: Tuesday, August 21, 2018 4:03:18 AM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] Tonix TNX-102 SL Phase 3 Poster - Time since trauma

Dear [redacted]

We're presenting topline and some retrospective analyses of Phase 3 for TNX-102 SL (sublingual cyclobenzaprine) today at the Military Health System Research Symposium. The P3 missed its primary endpoint, but we saw an important effect of time-since-trauma. PTSD ≤9 years since trauma responded, but PTSD >9 years didn't. Nine years was the approximate median time-since-trauma for the P3 cohort. Our Phase 2 study had a median time-since-trauma of only 6 years and we had relatively few participants >9 years. So the <9 year subgroup of P3 replicated the response results of P2. We don't know more about the responders/non-responders yet, but the ≤9 years group may have more people in the "remitting" phase of PTSD and the >9 years group may have more people in the "persistent" phase (ie, *Kessler et al. Arch Gen Psychiatry 1995;52:1048-1060*). One of the mechanisms of cyclobenzaprine is antagonism of α2. It's interesting that Raskind's + and – prazosin studies were conducted on predominantly <9 and >9 year cohorts, respectively (*Raskind et al. NEJM* 2018;378:507-517 and *Raskind et al. Am J Psychiatry* 2013;170:1003-1010). I've attached a copy of the poster and the press release.

We're interested in your thoughts.

[redacted]

[redacted]

[redacted] [redacted] >
Sent: Saturday, February 2, 2019 4:56 AM
To: [redacted]
Subject: [EXTERNAL] [redacted] joined Allergan

[redacted]

I believe that T[redacted] is now acting director of the division of Psychiatric Products. Allergan is working on rapastinel (https://en.wikipedia.org/wiki/Rapastinel) – a glutamatergic drug from Naurex.

https://www.linkedin.com/in/mitchell-mathis-62b833103/

[redacted]

[redacted]

From: [redacted]
Sent: Thursday, August 9, 2018 7:03 PM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] brexpiprazole phase 3 for PTSD

H[redacted]

Hope you had a great summer! Glad to see that we are now fully enrolled and will see some results hopefully before Christmas!

As part of our continuing efforts to identify VA sites for a potential Phase 3 program, we met with [redacted] and [redacted], head of the [redacted] at the [redacted]. [redacted] indicated she would be willing to help streamline the CREDA/IRB process with other VA sites who have done research in PTSD to help the brexpiprazole phase 3 program. She indicated they have the resources and we were wondering your thoughts on working with a local VA such as the [redacted] to increase VA site participation? Does it make sense as a way to break down bureaucracy?

And assuming the results are positive, we hope we can count on you as to continue as PI of the program as you have already done so much…and data is only a few months away!!

Please let us know; we can set up a call to discuss if would like.

[redacted]

From: [redacted]
Sent: [redacted]
To: [redacted]

Cc: [redacted]

Subject: [EXTERNAL] [redacted] February Steering Committee Call Minutes & Pharmaceutical Pipeline Information
Attachments: [redacted].pdf; Pipeline_Outreach.xlsx

Dear [redacted] Steering Committee,

Please see the attached [redacted] Steering Committee February Call Minutes. I have also included the Pharmaceutical Pipeline Call for Proposals and the contact list for the targeted pharmaceutical pipeline emails. To date, ASCP has received pharmaceutical pipeline abstracts from [redacted] Please feel free to distribute this call for proposals and/or email me with any individuals that you would like me to contact.

Please note that the pharmaceutical pipeline submission deadline has been extended to **Monday, March 12, 2018**.

As a reminder, the next scheduled [redacted] Steering Committee Call is **Wednesday, March 07, 2018 from 3:00 PM – 4:00 PM eastern time**.

[redacted]

[redacted]

From: [redacted]
Sent: Thursday, March 16, 2017 11:38 AM
To: [redacted]
Subject: [EXTERNAL] RE: a different study

Hi, [redacted] You are a grant-writing machine! Holy smokes---makes me tired just thinking about it. I would be happy to do the CAPS-5 training, and also have a couple of excellent colleagues who have been helping me with the Tonix and Otsuka trials (including IMs and rater evaluations). The basic rates are:

1. $1500/day for IMs, including a .5 day for travel.

2. $300 per CAPS-5 review (initial mock or fidelity)

3. $150/hour for other study-related activities (although I don't charge for stuff like planning/coordination phone calls, etc.)

Re: fidelity, first, a lot of studies don't even bother, other than initial certification, so if budget is tight you won't be out of the norm not to do it at all. If you have money to do it, I would say do the first real interview, and then maybe two or three more per rater over the course of the study. A good, inexpensive way to enhance and maintain training is to set up scoring calibration exercises where everyone listens to the same interview, makes independent ratings, and then checks their ratings against expert consensus scores.

Also, I strongly recommend creating scripts for mock respondents to use, so that role-played responses are consistent and plausible. We wrote a bunch for Tonix for the current study and it has made a world of difference. It also allows us to develop expert consensus scores to get a more objective assessment of raters' scoring skill.

Hope this helps! Thanks, [redacted]

From: [redacted]
Sent: Thursday, March 16, 2017 9:41 AM
To: [redacted]
Subject: a different study

[redacted]

I am submitting an LOI and preliminary budget for a randomized placebo controlled study of a new drug in patients with Alcohol use disorder and comorbid PTSD. Alcohol use is the primary outcome and the CAPS is the secondary outcome. This is a Dept of Defense grant.

I would like to invite you to be the CAPS trainer at the study start-up and certify the raters.

If budget allows, we can also do CAPS rater fidelity monitoring.

There will be 7 sites (very experienced investigators, but the independent CAPS raters may have varying degree of experience). Each site will have an independent rater and likely a back-up rater, so certification for 14 raters.

The enrollment will be over an 18 month period , randomizing about 250 patients. The training period will be sometime at the end of 2017

So my question to you:

Do you have time to help me with this study?

What should I budget for the training (start-up meeting) and rater certification aspect?

What should I budget for the fidelity monitoring (7 sites with a CAPS review for each rater for a couple of the first patients entered and then again at a midpoint; or what would you suggest?)

Thanks for your consideration,

[redacted]

[redacted]

From: [redacted]
Sent: Friday, February 15, 2019 9:30 AM
To: [redacted]
Subject: [EXTERNAL] RE: Update?

Dear [redacted],

Great. I'll be on my cell [redacted]. Should I call you or will you call me?

[redacted]

From: [redacted]
Sent: Friday, February 15, 2019 9:42 AM
To: [redacted]
Subject: RE: Update?

415 ET is fine, looking forward to catching up. Hope your study launch was successful.

From: [redacted]
Sent: Thursday, February 14, 2019 4:39 PM
To: [redacted]
Subject: [EXTERNAL] RE: Update?

Dear [redacted]

I'm available 4:15 pm – 6:15 pm ET. Do you have time in that window?

[redacted]

From: [redacted]
Sent: Thursday, February 14, 2019 5:37 PM
To: [redacted]
Subject: RE: Update?

Tomorrow afternoon

[redacted]

From: [redacted]
Sent: Thursday, February 14, 2019 7:07 AM
To: [redacted]
Subject: [EXTERNAL] Update?

Dear [redacted]

Let’s speak on the phone about the status of the grant/trial. What are good times?

[redacted]

[redacted].com>
Sent: Tuesday, March 6, 2018 12:22 PM
To: [redacted]
Subject: [EXTERNAL] References we discussed
Attachments: Stefanovics EA Minimal Clinically Important PTSD Psychiatr Q - 10.1007_s11126-017-9522-y.pdf; Weathers CAPS-5 2017-20898-001.pdf

[redacted]

References we discussed.

[redacted]

Minimal Clinically Important Differences (MCID) in Assessing Outcomes of Post-Traumatic Stress Disorder.

Stefanovics EA[1,2], Rosenheck RA[3,4], Jones KM[5], Huang G[6], Krystal JH[3,4,7].

Author information

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6
VA Cooperative Studies Program Central Office, Washington, D.C, USA.
7
Clinical Neuroscience Division, Department of Veterans Affairs National Center for PTSD, West Haven, CT, USA.

Abstract

This study sought to determine the minimal clinically important difference (MCID) for two frequently used measures of symptom severity in Post-Traumatic Stress Disorder: the Clinician Administered PTSD Scale

(CAPS) and the PTSD Symptom Checklist (PCL). Data from a randomized clinical trial of antipsychotic medication in military-related treatment-resistant PTSD (N= 267) included assessments 4 times over 26 weeks. Methods for estimating the MCID were based on both the anchor-based approach, using the Clinical Global Impressions (CGI) severity and improvement scales, rated by both clinicians and patients; and the distribution-based approach (based on standardized z-scores). Severity and change scores on the CAPS and PCL were converted to z-scores and compared across CGI levels using analysis of variance. The average difference in CAPS z-scores between each of three CGI levels between "moderate" to "severe" and from "no change" to "much improved" was 0.758 for clinician CGI ratings and 0.525 for patient CGI ratings and were similar for the PCL (0.483 and 0.471) with all differences significant at p<.0001). Clinically meaningful CAPS and PCL severity and change z-scores range between 0.5-0.8 standard deviations. The MCID estimates suggested here provide an empirical basis for determining whether statistically significant changes in CAPS and PCL scores are clinically meaningful.

KEYWORDS:

Minimal clinically important difference; Outcome assessment; PTSD

PMID:
28634644
DOI:
10.1007/s11126-017-9522-y
Psychol Assess. 2017 May 11. doi: 10.1037/pas0000486. [Epub ahead of print]

The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5): Development and Initial Psychometric Evaluation in Military Veterans.

Weathers FW, Bovin MJ, Lee DJ, Sloan DM, Schnurr PP, Kaloupek DG, Keane TM, Marx BP.

Abstract

The Clinician-Administered PTSD Scale (CAPS) is an extensively validated and widely used structured diagnostic interview for posttraumatic stress disorder (PTSD). The CAPS was recently revised to correspond with PTSD criteria in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013). This article describes the development of the CAPS for DSM-5 (CAPS-5) and presents the results of an initial psychometric evaluation of CAPS-5 scores in 2 samples of military veterans (Ns = 165 and 207). CAPS-5 diagnosis demonstrated strong interrater reliability (κ = .78 to 1.00, depending on the scoring rule) and test-retest reliability (κ = .83), as well as strong correspondence with a diagnosis based on the CAPS for DSM-IV (CAPS-IV; κ = .84 when optimally calibrated). CAPS-5 total severity score demonstrated high internal consistency (α = .88) and interrater reliability (ICC = .91) and good test-retest reliability (ICC = .78). It also demonstrated good convergent validity with total severity score on the CAPS-IV (r = .83) and PTSD Checklist for DSM-5 (r = .66) and good discriminant validity with measures of anxiety, depression, somatization, functional impairment, psychopathy, and alcohol abuse (rs = .02 to .54). Overall, these results indicate that the CAPS-5 is a psychometrically sound measure of DSM-5 PTSD diagnosis and symptom severity. Importantly, the CAPS-5 strongly corresponds with the CAPS-IV, which suggests that backward compatibility with the CAPS-IV was maintained and that the CAPS-5 provides continuity in evidence-based assessment of PTSD in the transition from DSM-IV to DSM-5 criteria. (PsycINFO Database Record.

PMID:
28493729
PMCID:
PMC5805662
[Available on 2018-11-11]
DOI:
10.1037/pas0000486
Share

[redacted]

From: [redacted]
[redacted] Tuesday, July 18, 2017 8:45 AM
To: [redacted]
[redacted]
Subject: [EXTERNAL] NDAA Committee report - Senate Armed Services Committee

Dear [redacted]

Here's a link to relevant language in the Senate Armed Services report:

[redacted]

S. Rept. 115-125 - NATIONAL DEFENSE AUTHORIZATION ACT FOR FISCAL YEAR 2018**115th Congress (2017-2018)**

Senate Armed Services Committee – "Committee Report", p. 173

"Novel drug therapies for PTSD

The committee has long supported the development of new therapies for the treatment of post-traumatic stress disorder (PTSD). The committee urges the Department to prioritize the development and approval of novel drug therapies for the treatment of PTSD. To accomplish this task, the committee encourages the Department to consider the Food and Drug Administration's (FDA) Breakthrough Therapy Designation program. This program is one of four FDA programs intended to help ensure rapid approval and availability of beneficial therapies for serious medical conditions. The Committee directs the Department to consider carefully any guidance that the FDA's Breakthrough Therapy program may provide for the identification, development, and approval of novel therapies for the treatment of PTSD."

I'll look for the other email.

[redacted]

[redacted]

From: [redacted]
Sent: Monday, April 29, 2019 3:47 PM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] RE: Simple trauma-focused therapy

Dear [redacted]

Please send us the paper about the simpler version of trauma-focused therapy.

[redacted]

From: [redacted]
Sent: Monday, March 25, 2019 7:03 PM
To: [redacted]
Cc: [redacted]
Subject: Simple trauma-focused therapy

Dear [redacted]

We are speaking with [redacted] (copied) about her interest in doing a PTSD study in vets using a randomized withdrawal design. We are discussing whether it should be a straight drug study or if it should be "drug assisted psychotherapy". If it's drug assisted psychotherapy, we think that Prolonged Exposure is too onerous and expensive – similar to your views on this topic when we discussed it on the phone recently. We'd be interested in the citation for the study that showed a one-paragraph trauma-focused therapy was similar or non-inferior to PE. Please send it.

Also, we'd like to start including you in this dialogue and planning.

[redacted]

[redacted]

From: [redacted]
[redacted] Monday, January 29, 2018 8:39 AM
To: [redacted]
[redacted]
Subject: [EXTERNAL] Discuss studies on VA patients - Thursday, Feb 1 from 10:30 am - 11:30 am ET

Dear [redacted],

I invited [redacted] (copied) and fortunately, she's available to join the call on Thursday, Feb 1 from 10:30 am - 11:30 am ET.

Please use [redacted]

[redacted] thank you for correcting my "fat finger" mistake about sending out a calendar invite for Wednesday instead of Thursday. I hope it's straight in everyone's calendar now.

Best, Seth

[redacted]

[redacted]

Sent: Tuesday, August 21, 2018 12:49 PM
To: [redacted]
Subject: [EXTERNAL] Re: Tonix TNX-102 SL Phase 3 Poster - Time since trauma

Here's what I sent:

Hi [redacted],

This is really interesting. My immediate take is that time since trauma is not necessarily the driver. I would have wanted to see comparisons between the two groups on a variety of potentially causal factors. I also would love to see a scatterplot of pre-post change vs. time since trauma.

9 years is still a very long time to have PTSD, so it seems a bit arbitrary to pick that number just because it was your median. Technically PTSD is chronic much earlier, and I think it you defined is outside of the DSM, something like 3-5 years would be a better number.

I recommend better trying to understand the factors that modify treatment outcome in the data, to better isolate what is going on.

We had a separate thread to discuss this because [redacted] sent to the PTSD Psychopharm group. I second the point that [redacted] made about the effects being present at 4 weeks—odd that placebo seems to continue to catch up a bit.

Glad to get on a call to brainstorm. As I said, this is very interesting.

[redacted]

P.S. I don't make much out of the old [redacted] data because it is really old and retrospective

---

From: [redacted]
Date: Tuesday, August 21, 2018 at 11:43 AM
To: [redacted]
Subject: Re: Tonix TNX-102 SL Phase 3 Poster - Time since trauma

I had some similar thoughts. I shared the following comments with [redacted]

Hi [redacted]

I had a few thoughts looking at the data.

First, that the striking difference in trauma history was the relative absence of recent trauma (<4 yr) in 301 relative to 201 as opposed to the overall 3-4 yr difference in median time since trauma. I doubt that difference is meaningful. Questions for you include: 1) what symptoms were most prominent in the very recent trauma group? 2) what symptoms changed the most in that group? And 3) was there evidence of a meaningful clinical effect in that group (improvement in caps correlate with CGI?, etc.).

Second, your overall effect size (0.36) is not bad, but your study was underpowered significantly to detect this.

Third, the effects of your drug seem to be evident maximally within 4 weeks. The additional 8 weeks of treatment did not produce additional benefit. The way that this affected your outcome was that the placebo group for the >9 years since trauma subgroup progressively improved over the study, undermining your power to detect a treatment effect (particularly with a linear model). Interestingly, this is different that what we saw with risperidone, where the magnitude of the drug-placebo difference grew progressively over time.

Fourth, I wondered about the robustness of effects on sleep vs overall PTSD symptom severity. Were they correlated?

Looking forward to talking,

[redacted]

On Aug 21, 2018, at 7:13 AM, [redacted] wrote:

Hl [redacted]

Thank you for sharing the data. I look forward to reviewing it more closely. I'm sorry that you did not hit your primary endpoint. Did you evaluate the relationship between time from trauma and magnitude of clinical improvement? That would help to determine whether there was an overall relationship between these variables. Particularly in the absence of a strong a priori hypotheses, these sorts of secondary analyses can be very misleading.

Best,

[redacted]

From: [redacted]
[redacted]:39 AM
To: [redacted]
Cc: [redacted]
Subject: Re: Tonix TNX-102 SL Phase 3 Poster - Time since trauma

[redacted] and [redacted] also sent me the poster and their press release this morning. Here's what I said to them:

Hi [redacted] and [redacted].

Interesting finding. It makes some sense that the more chronic the PTSD, the more unlikely it is to respond to treatment… though I've never seen data before supporting this supposition.

I have been recommending to pharma companies doing PTSD trials that they limit duration of PTSD to 10 years. These findings suggest that might not be a bad idea.

I'd like to see some sensitivity analyses at other duration cut points. Does this only work at 9 years? How about 8? Or 10?

Best,

[redacted]

From: [redacted]
Date: Tuesday, August 21, 2018 at 4:12 AM
To: [redacted]
Subject: FW: Tonix TNX-102 SL Phase 3 Poster - Time since trauma

Hello Everyone,
I thought all would be interested in the Tonix trial release and poster that is being presented today at the Military Health System Research Symposium. [redacted] I will be talking with [redacted] next week regarding results and potential for any further study.
As always, comments are welcome,

Best,
[redacted]

[redacted]

[redacted]
Sent: Thursday, February 2, 2017 1:13 PM
To: [redacted]
[redacted] [EXTERNAL] RE: Time to have a call tomorrow?

Yes, why don't we say 11am Central/ Noon EST? I'll be at my desk at [redacted]

Best,

[redacted]

From: [redacted]
Sent: Thursday, February 2, 2017 1:24 PM
To: [redacted]
Subject: Time to have a call tomorrow?

[redacted], are you available tomorrow to have a call with just me to go over the strategy, timeline and materials that we need to write or obtain from other

[redacted]

From: [redacted]
Sent:
To: [redacted]
Subject: rtunate headline

Dear [redacted]

An unfortunate Fox Business headline about [redacted]:

[redacted]

Anyway, in the article, the Army is quoted as saying,

> "The Pentagon 'is committed to discovering, developing, and deploying the best medical solutions to treat PTSD," she said in an emailed statement. "Our current focus is using an innovative clinical trial design for Phase 2 testing of multiple drugs simultaneously, as opposed to the traditional one-drug-at a time approach.'"

This is referring to the [redacted] study. Really?

[redacted]

[redacted]

From: [redacted]
Sent: Thursday, November 1, 2018 4:19 AM
To: [redacted]
Subject: [EXTERNAL] FW: USAMMDA awarded $26 M to UCSF for TBI consortium - PTSD RFP expected
Attachments: Drug Treatment for Traumatic Brain Injury (DTTBI) - MTEC.pdf

Dear [redacted]

I realized that it was very "defeatist" to think that this CVB award was in lieu of the PTSD clinical consortium RFP. If we take that "defeatist" view, then CVB will also swoop in and get the PTSD consortium RFP if and when that materializes. A much more pro-active approach is to assume that the CVB award was different and to position us with top PTSD investigators to put in a proposal if/when the RFP for the consortium materializes.

[redacted]

From: [redacted]
Sent: Thursday, November 1, 2018 5:16 AM
To: [redacted]
Subject: USAMMDA awarded $26 M to UCSF for TBI consortium - PTSD RFP expected

Dear [redacted] and [redacted]

I look forward to discussing our PTSD trial. I also would like to discuss ways we might work together on future projects.

I think there is federal money, particularly DoD money, that is or will be available for PTSD research, but universities and industry have not been effective in working together to get it.

You may or may not follow USAMMDA's interest in PTSD and TBI. Almost two years ago, USAMMDA issued an RFP for a TBI consortium and they JUST announced the winner – a consortium led by UCSF (see attached). This consortium does not appear to have an industry partner – but I don't know whether industry is focused on TBI.

USAMMDA/MTEC have previously told us (and said publicly) that they are going to issue a very similar RFP for a PTSD consortium. I monitor the website (of MTEC) and I have not seen it issued yet. But since the timelines are short once the RFP is issued, I think it would be useful to think about whether your group/institution might lead or participate in such an effort/proposal and whether and how we (Tonix) might be involved.

USAMMDA has money. [redacted] just announced (see below) that USAMMDA just awarded them $29 M to conduct a PTSD drug trial. As I understand it, their plan is to study two drugs (phase 2 drugs) against a placebo or an SSRI in a three arm trial with 450 military-PTSD patients. Also, they are planning to do extensive testing (imaging, genetic analysis, transcription analysis, etc.). CVB got this money using the USAMMDA/MTEC multi-topic solicitation.

While this award may put CVB in a good position for the consortium award, I think your groups would also be well positioned. I would like to discuss whether we could be a useful partner/member of consortium/co-investigator – or something. We have a lot of drug development experience in PTSD (500 military PTSD patients studied in two registration-quality trials) and we have capital for matching funds (which the gov't likes). (As I understand it, CVB did not have to make any commitment for matching funds.)

I look forward to speaking.

Cohen Veterans Bioscience Receives Research Award from Department of Defense's Medical Research and Materiel Command to Establish A Clinical Trial Infrastructure and Conduct an Adaptive Platform Trial Testing Post-Traumatic Stress Disorder (PTSD) Pharmacotherapeutics

CAMBRIDGE, Mass., Oct. 4, 2018 – Cohen Veterans Bioscience, a Cambridge, MA based 501c3 non-profit research organization will establish a clinical trial infrastructure and serve as the Clinical Coordinating Center for a 3.5-year study to comparatively test pharmacotherapeutics for PTSD under an award managed by Advanced Technology International (MTEC Consortium Manager) on behalf of the U.S. Army Medical Research and Materiel Command (MRMC).

PTSD is a mental health condition that some people develop after experiencing or witnessing a violent or life-threatening event, such as combat, natural disaster, terrorist attack, or sexual assault. Symptoms of PTSD can include reliving the event or having flashbacks; avoiding situations that trigger the memories; losing interest in activities or feelings of fear, guilt, or shame; feeling anxious or always on alert for danger. PTSD affects about 7.7 million American adults each year and is the fifth most prevalent mental disorder in the United States. Overall prevalence rates among veterans of different conflicts range from 10-30% (OEF/OIF/OND/Gulf War/Vietnam).

The only approved medications for the treatment of PTSD are the selective serotonin reuptake inhibitors (SSRIs) sertraline (Zoloft®) and paroxetine (Paxil®) approved over 17 years ago. The Department of Veteran Affairs (VA) 2017 Consensus Statement of the PTSD Psychopharmacology Working Group concluded that there is a deficient pipeline of new PTSD medications and an assessment of recent trial failures has generated concerns about how to best identify new targets for medication development and optimally design clinical studies. In a highly heterogeneous patient population such as PTSD, the availability of validated biomarkers or companion diagnostics would allow clinicians to predict the likelihood that a given patient would respond to a given therapeutic, enabling

individualized medicine for these conditions. No biomarkers have been qualified nor cleared as companion diagnostics for PTSD by the Food and Drug Administration.

Most critically, the field has historically conducted the majority of clinical trials using "traditional trial design" approaches. These approaches are generally time-consuming, have been associated with high failure rates, and are expensive, as they often result in starting over in a new trial with lessons learned.

CVB will be spearheading the design and application of "Smart-" or "Adaptive-" clinical trials for PTSD. These studies include a *prospectively* planned opportunity for modification of one or more specified aspects of the study design based on data (usually interim data) collected from subjects in the study. To execute such a program, a centrally-managed platform clinical trial infrastructure will be established, potentially including academic, private, VA, and military research centers.

"Advancing our understanding of disease while promoting a precision medicine approach for the treatment of PTSD is fundamentally important to help us support our mission to protect, treat and sustain the health of Service Members," said Dr. Kimberly A. del Carmen, who will serve as Sponsor Office Technical Representative on behalf of the U.S. Army Medical Materiel Development Activity Neurotrauma and Psychological Health Project Management Office.

"The unique and innovative aspects of an adaptive platform trial approach for testing therapeutics for PTSD is in the ability to capitalize on the information you gather while the study is ongoing," said Allyson Gage, PhD, Chief Medical Officer at CVB and Head of the Adaptive Trial Program. "Clinical trial networks capable of conducting these trials with high fidelity is a critical piece of de-risking drug development in psychiatric trauma-related conditions."

About Cohen Veterans Bioscience

Cohen Veterans Bioscience is a national, nonpartisan research 501(c)(3) organization dedicated to fast-tracking the development of diagnostic tests and personalized therapeutics for the millions of veterans and civilians who suffer the devastating effects of trauma-related and other brain disorders. To support & learn more about our research efforts, visit www.cohenveteransbioscience.org.

For media inquiries, please contact:

media@cohenbio.org

View this press release on PR Newswire

[redacted]

From: [redacted]
Sent: Wednesday, March 20, 2019 1:20 PM
To: [redacted]
Subject: RE: [EXTERNAL] We lost you…

Monday any of those times work for me

From: [redacted]
Sent: Wednesday, March 20, 2019 1:16 PM
To: [redacted]

[redacted] how about 3pm, 3:30pm, 4pm, 4:30pm?

Best,
[redacted]

[redacted]

From: [redacted]
Sent: Wednesday, March 20, 2019 12:19 AM
To: [redacted]
Subject: RE: [EXTERNAL] We lost you...

Monday afternoon works for me except for 2-3 pm ET/1-2 pm CT for a call with [redacted] and [redacted]

[redacted] – Let's keep the Friday call so you and I can catch up.

From: [redacted]
To: [redacted]
Subject: RE: [EXTERNAL] We lost you...

Sure, Monday afternoon is great for me.

[redacted]

From: [redacted]
Date: Tuesday, Mar 19, 2019, 7:58 PM
To: [redacted]
Subject: RE: [EXTERNAL] We lost you...

I'll be in the air on Friday. May we do the Monday time instead?

[redacted]

From: [redacted]
Sent: Tuesday, March 19, 2019 11:11 AM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] We lost you...

Dear [redacted]

[redacted] is on the West Coast so let's use [redacted]

[redacted]

From: [redacted]
Sent: Tuesday, March 19, 2019 1:20 PM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] We lost you...

OK, call me at [redacted]

[redacted]

From: [redacted]
Sent: Tuesday, March 19, 2019 12:14 PM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] We lost you...

Let's speak 11:30 – noon CT on Friday.

From: [redacted]
Sent: Tuesday, March 19, 2019 1:11 PM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] We lost you...

I'm back and can find time to chat on Friday 1130 to 1230 central or next Monday

[redacted]

From: [redacted]
Sent: Tuesday, March 19, 2019 11:59 AM
To: [redacted]
Subject: RE: [EXTERNAL] We lost you...

Dear [redacted]

I lost track. Are you back this week or not until next week?

[redacted]

From: [redacted]
Sent: Saturday, March 2, 2019 11:40 AM
To: [redacted]
Cc: [redacted]
Subject: RE: [EXTERNAL] We lost you...

Yep, I lost you in the elevator and didn't have the call in number with me. Sorry about that.

I'm off to the Turks and Caicos right now with family and get back in office next Friday but will be on all day grant review committee on Friday, so next week is best. I will follow up on Friday to get a time scheduled

Thanks

[redacted]

From: [redacted]
Date: Saturday, Mar 02, 2019, 9:55 AM
To: [redacted]
Cc: [redacted]
Subject: [EXTERNAL] We lost you...

Dear [redacted]

We lost you on the call. We hope all's well. We were wondering if we should put out an APB to find you in that elevator.

We were pleased that [redacted] is excited about a "drug assisted psychotherapy" trial/project/grant for TNX-102 SL. Let's discuss whether it makes sense to do a 10 patient open label study. We agree with you, that Tonix has >500 patents treated.

I'm okay with [redacted] idea that we only have two group: PE/placebo v. PE/TNX-102 SL. If TNX-102 SL shows an advantage over placebo, then someday we could do a 2x2 trial with the other two conditions head to head (ie, medication management/placebo and medication management/TNX-102 SL.)

Even the simpler study would test the hypothesis that TNX-102 SL enhances the effects of PE.

Let’s find a time to talk.